UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/685,053	10/06/2000	David M. Armistead	A-748E	3146

7590 05/01/2003

U.S. PATENT OPERATIONS/JWB
AMGEN INC. - M/S 27-4-A
ONE AMGEN CENTER DRIVE
THOUSAND OAKS, CA 91320-1799

EXAMINER
BALASUBRAMANIAN, VENKATARAMAN

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 05/01/2003

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/685,053	Applicant(s) ARMISTEAD ET AL.	
	Examiner Venkataraman Balasubramanian	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10-29 and 32-35* is/are pending in the application.

4a) Of the above claim(s) *32-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 10-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6 &10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants' response, which included cancellation of claims 8-9, amendment to claims 1, 6, 22, 24-27 and addition of new claims 32-35, filed on 2/5/2003, is made of record.

Newly submitted claims 32-35 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Whereas originally submitted method of use claims relied on kinase activity of the instant compounds, the newly added claims as recited include any or all mode of action. Hence the scope of the newly added claims is different from the scope of originally presented method of use claims. If these claims were presented originally the invention would have been subjected restriction requirement.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 32-35 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-7 and 10-29 are active in the application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 and 10-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The amendment to claims 1, 6, 22 and 24-27 by inserting provisos at the last line of these claims is deemed as introducing new matter. These amended claims now recite " provided R^1 and R^2 are not both 1-alkylpyridinium and both 4-pyridyl; further provided neither R^1 or R^2 is morpholino or amino" which introduces limitations in the variables R^1 and R^2 choices. But the originally presented claims R^1 and R^2 are independent varible and can be chosen irrespective what the other group is. TA new concept in varying R^1 and R^2 is introduced and thus the scope of the amended claims was not same.

In view of applicants' response, the following rejections made in the previous office action remain.

Claims 24-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating angiogenesis, does not reasonably provide enablement for treating all diseases embraced in the claim language of the instant invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to 'a method for treating kinase–mediated disease or disease symptoms. Method claims 24-26 are not adequately enabled for the range of diseases recited therein. From the reading of specification, it appears that the

applicants are asserting that the embraced compounds because of their mode action, which involves inhibition of kinase(s), would be useful for all sorts of diseases including autoimmune diseases, cancer, Alzheimer's disease, various arthritis, multiple sclerosis etc. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by the claim language for the intended mammal. That a single class of compounds can be used to treat all diseases embraced in the claims is an incredible finding for which applicants have not provided supporting evidence. Moreover many if not most of diseases such as rheumatoid arthritis, multiple sclerosis, Alzheimer's disease etc. are very difficult to treat and hardly possible to prevent as claimed herein. For multiple sclerosis alone there is no known drug, which can successfully reverse the course of the disease, despite the fact that there are many drugs, which can be used for "inflammatory condition". Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288 . Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses. Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed 'preventive' effect solely based on the inhibitory activity disclosed for the compounds.

The state of the art is indicative of the requirement for undue experimentation. See Traxler (provided).

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic use of the compounds in treating all diseases due to kinase inhibitory activity.

2) The state of the prior art: Although there are several kinase inhibitors known, they have not been able to treat all diseases embraced in the instant claims.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for the 'treatment of all kinase mediated diseases' of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: There is no supporting evidence that all diseases embraced are treatable in view of their kinase activity.

6) The breadth of the claims: The instant claims embrace treatment of all or any diseases by inhibiting all or any kinase

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards 'preventing' the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

This rejection is same as made in the previous office action. Applicants' argument to overcome this rejection is not persuasive. Following apply.

1. First of all, applicants' traversal of the rejection by providing references is deemed as improper as it does no meet the criteria of "at the time the instant invention was made". All references cited do not strictly qualify as prior art.

2. As noted before, the examiner had provided a proper prior art, Traxeler, which clearly states the art at the time of the instant invention was made is still exploratory.

Hence the rejection is proper and is maintained.

The following rejections made in the previous office action are also maintained, as the provisos in the amended claims are not applicable.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, 8 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Giraldi et al. US 3,074,943.

Giraldi et al. teaches several substituted triazines for use as anti viral agents, which include compounds generically claimed in the instant claims. See formula I and note the definition of R', R", and R"' on col.1. Note when R"' is hydrogen, the compounds taught by Giraldi include those claimed in the instant claims. See examples 1-5 for compounds made and the intermediates used for making on col.2-3.

Claims 1, 5-8, 22 and 30-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Cutler et al. US 3,097,205.

Cutler et al. teaches several disubtituted triazines, which include those, claimed in the instant claims for use as antibacterial agents. See formula I, III, IV, V, VI, VII and

VII and note the definition of Y, Z and Z' on col. 1 through col. 3. Note the definition of Y, Z and Z' corresponds to instant R^1 and R^2. Also note the various choices of Z and Z' on col.2 and the process of making. See col. 3 –col.9 for examples of compounds made.

Claims 1, 6 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Cutler et al. US 3,209,003

Cutler et al. teaches several disubtituted triazines, which include those, claimed in the instant claims for use as antibacterial, antifungal and antiviral agents. See formula I and note the definition of X, R, Y^1 and Y^2 on col.1. Note the definition of X, R, Y^1 and Y^2 corresponds to compounds of instant R^1 and R^2. See examples 1-25 for various compounds made shown on col. 5 through 11.

Claims 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Fischer US 3,855,220.

Fischer teaches pyridinium- triazine and its intermediates which are also generically embraced in the instant claim. See compound of formula I and II on col. 1-2 and col. 4 and example 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 6, 8-9 and 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Newton et al. US 5,062,882.

Newton et al. teaches several substituted triazines for use as herbicides. See formula I on col. 1 and note the definition of X, Y, Z, R1 and R^2. Note when one of R^1 and R^2 group is hydrogen, the compounds taught by Newton et al. include those claimed in the instant claims. See examples 1-72 on col.5-18 for compounds made.

Instant claims recite disubstituted triazine, i.e. the third substituent on the triazine carbon is hydrogen. Newton et al. does not teach hydrogen for either of R^1 and R^2 in compounds made.

However Newton et al. teaches the equivalency of exemplified substituents for R^1 and R^2 groups with that claimed. See cols.1, formula I, especially the definitions of R^1 and R^2 groups. As one trained in the art would expect the species of the genus behave similarly and possess the same use, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted in triazine ring including species bearing hydrogen for R^1 or R2 group as permitted by the reference and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Claims 1, 6, 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Riebel et al. US 6,284,710 (equivalent DE 196 41 693).

Riebel et al. teaches several substituted triazines for use as herbicides. See formula I on col. 1 and note the definition of X, Y, Z, R^1 and R^2. Note when Z is hydrogen, compounds taught by Riebel et al. include those claimed in the instant claims. See col. 6 through col. 58 for compounds made.

Instant claims recite disubstituted triazine, i.e. the third substituent on the triazine carbon is hydrogen. Riebel et al. does not teach hydrogen for Z in compounds made.

However Riebel et al. teaches the equivalency of exemplified substituents for Z groups with that claimed. See cols.1, formula I, especially the definition Z groups. As one trained in the art would expect the species of the genus behave similarly and possess the same use, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted in triazine ring including species bearing hydrogen for Z group as permitted by the reference and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

As note above all these rejections are same as made in the previous office action and are maintained as the proviso in the amended claims are not applicable.

References cited in the Information Disclosure Statement (paper # 6 &10) are made of record.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (703) 305-1674. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (703) 308-4716.

The fax phone number for the organization where this application or proceeding is assigned (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

VB
V. Balasubramanian

4/28/2003

Mukund J. Shah
MUKUND J. SHAH
SUPERVISORY PATENT EXAMINER
AU 1624